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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,400	09/20/2005	Kenji Sato	HOP03167US0	9280

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EXAMINER	
GUSSOW, ANNE	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/574,400	SATO ET AL.	
	Examiner	Art Unit	
	Anne M. Gussow	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-11 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 20 September 2005 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 4/3/2006.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-11 are pending in this application.

Specification

1. The amendment filed April 25, 2006 has been entered.

2. The disclosure is objected to because of the following informalities:

a). The description of the figures does not adequately describe the figures to allow one to understand the results being displayed. In particular, in figure 11, what is the protein pointed out by the arrow. Also, figure 8A, what are the arrows for.

b). Typographical errors, for example page 5 paragraph 27, inhibiging should read inhibiting.

Appropriate correction is required.

3. The use of the trademark Superdex® has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the description of the main component of the isolated proteoglycan. Claim 1 recites an isolated proteoglycan, does main component mean the proteoglycan or is there a composition containing the isolated proteoglycan.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for reciting "improvement in quality of life" because the exact meaning of the phrase is unclear. Improvement in quality of life could be interpreted to mean lengthening life span, relieving pain, or improving function, for example.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated proteoglycan derived from a water extract of cartilage using a particular method which consists of pulverizing cartilaginous fish-derived cartilage to a specified average diameter, adding water to the product, separating the aqueous phase, and adding alcohol to the aqueous phase to obtain a precipitate, whose main component is a proteoglycan of 500

kDa molecular weight. While the extraction method is adequately described in the specification, there is insufficient written description as to the identity of the proteoglycan product.

The specification as filed does not provide adequate written description support for a specific proteoglycan. Thus a broad genus having potentially highly diverse functions is encompassed by the phrase 500 kDa molecular weight and conception cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. For example, Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., Abstract and Sequence-based approaches to function prediction, page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein. In addition, the additional limitations of activity do not add to the written description because it is not clear from the specification if the proteoglycan is a single species or a component of many species. The specification does not describe complete isolation of the proteoglycan and only characterizes it by molecular weight and amino acid composition (see in particular Abstract and Box 2). Adequate written description requires more than a mere statement that it is part of the invention. The sequence itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Proteoglycans are a diverse group of heterogeneous macromolecules that include chondroitin sulfate, dermatan sulfate, heparin sulfate-heparin proteoglycans and aggregating proteoglycans (Kuettner and Kimura, Journal of Cellular Biochemistry 1985 Vol. 27 pages 327-336, particularly page 334 paragraphs 1 and 3). Therefore, a proteoglycan of 500 kDa does not meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed. (See page 1117.) The specification does not clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, & 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-10 are rejected under 35 U.S.C. 102(a) as being anticipated by Murata (Journal of Nara Medical Association, Vo. 53 No. 5-6, December 2002, pages 241-252).

The claims recite an isolated proteoglycan from water extract of shark cartilage in a pharmaceutical composition whose main component has a molecular weight of 500 kDa or more, is mainly composed of chondroitin sulfate C, has MMP-9 inhibiting activity, and increases haptoglobin in blood serum.

Murata teaches a water extract preparation of shark cartilage that has a main component of chondroitin sulfate and when administered to a hamster model suppresses MMP-9 activity and increases haptoglobin levels in blood serum.

The product of claim 1 is defined in terms of a proteoglycan product, water extract and molecular weight. Consequently, comparison of this product with the prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be related and conduct comparisons. Thus a lesser burden of proof is required to make out a case of anticipation for a product claimed in terms of a laboratory designation than when claimed in conventional fashion by its physical characteristics, structure or even in terms of the process by which it is made.

The prior art product is made the same way, for example, pulverizing cartilaginous fish-derived cartilage, adding distilled water, separating the aqueous portion, and adding ethanol to obtain a precipitate. The prior art inhibited MMP-9 activity both *in vitro* and *in vivo*. The prior art does not teach the

molecular weight, however, it is the Examiner's position that Murata has produced a water extract of shark cartilage having the same functional activities as the applicants. Therefore, it appears that Murata has produced a cartilage extract that is identical to the claimed proteoglycan of the cartilage extract. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed proteoglycan with extract of Murata, the burden of proof is upon the Applicants to show a distinction between the structural and functional characteristics of the claimed proteoglycan and the cartilage extract of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

8. Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Kralovec, et al. (WO 03/068249 A1, filed February 15, 2002).

The claim recites a method of producing a proteoglycan extract from shark cartilage by pulverizing the cartilage to an average particle diameter of 100 μm or less, adding water, separating the aqueous phase and precipitating with an alcohol.

Kralovec, et al. teach a method of isolating a proteoglycan extract from a shark by pulverizing the sample and adding water, with a number of possible subsequent steps one of which is separating the aqueous phase and precipitation with an alcohol (pages 9-13, particularly page 12 lines 14-20 and Method C pages 20-21). Kralovec, et al. also teach pulverizing the cartilage sample to an average particle size of 35 μm (page 18 lines 22-23).

Since the method steps of claim 11 are included in the method of Kralovec, et al., all the limitations of the claim have been met.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murata (Journal of Nara Medical Association, December 2002), in view of Kralovec, et al. (WO 03/068249 A1, filed February 15, 2002).

The claims recite an isolated proteoglycan from water extract of shark cartilage in a pharmaceutical composition, which is mainly composed of chondroitin sulfate C, has MMP-9 inhibiting activity, and increases haptoglobin in blood serum, and the method of producing the proteoglycan including the steps

of pulverizing the cartilage to a particle size less than 100 μm, adding water to the sample, isolating the aqueous phase, adding alcohol to the aqueous phase to obtain a precipitate.

Murata has been described supra. Murata teaches a water extract preparation of shark cartilage that has a main component of chondroitin sulfate and when administered to a hamster model suppresses MMP-9 activity and increases haptoglobin levels in blood serum. Murata also teaches the method of extraction from shark cartilage. Murata does not teach the particle size of pulverized shark cartilage. This deficiency is made up for in the teachings of Kralovec, et al.

Kralovec, et al. have been described supra. Kralovec, et al. teach a water extract preparation of shark cartilage that has been pulverized to an average particle size of 35 μm (page 18 lines 22-23).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an extract of shark cartilage of Murata with the particle size of Kralovec, et al. One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced the shark cartilage extract of Murata with the particle size of Kralovec, et al. because both Murata and Kralovec, et al. are preparing water extracts of shark cartilage. Murata and Kralovec, et al. share the same method steps for the initial isolation from shark cartilage, but the description of Kralovec, et al. provides the additional detail of particle size. Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention

was made to have used the particle size of Kralovec, et al. in the extract of Murata.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER